

WHAT IS CLAIMED IS:

5 1. A method for stimulating a systemic immune response to an antigen in a mammal comprising:

providing a liposomal preparation comprising lyophilized liposomes containing at least one antigen, wherein the liposomes have at least two sizes, before lyophilization, selected from small liposomes having a size, before lyophilization, of from about 20 nm to
10 about 1 micron, medium liposomes having a size, before lyophilization, of from about 1 micron to about 3 microns, and large liposomes having a size, before lyophilization, of from about 3 microns to about 20 microns; and

orally administering an effective amount of the liposomal preparation to a mammal,
15 whereby sufficient antigen containing liposomes are absorbed in the Peyer's patches of the gut of the mammal and are taken up by macrophages in the Peyer's patches to stimulate a systemic immune response.

20 2. A method as claimed in claim 1, wherein the liposomes are multi-lamellar before lyophilization.

3. A method as claimed in claim 1, wherein the liposomal preparation is contained with an enterically-coated capsule.

25 4. A method as claimed in claim 1 wherein the liposomal preparation comprises large liposomes and small liposomes.

5. A method as claimed in claim 1 wherein the liposomal preparation comprises large liposomes and medium liposomes.
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6. A method as claimed in claim 1 wherein the liposomal preparation comprises medium liposomes and small liposomes.

35 7. A method as claimed in claim 1 wherein the liposomal preparation comprises small, medium and large liposomes.

5 8. A method as claimed in claim 1 wherein the liposomal preparation comprises at least 5% by volume small liposomes, at least 10% by volume medium liposomes and at least 20% by volume large liposomes.

10 9. A method as claimed in claim 1 wherein the liposomal preparation comprises about 10% by volume small liposomes, about 25% by volume medium liposomes and about 65% by volume large liposomes.

15 10. A method as claimed in claim 1 wherein the liposomes comprise at least two different antigens.

20 11. A method as claimed in claim 1, wherein the liposomes comprise at least one antigen selected from the group consisting of inactivated HIV I and HIV II antigens.

25 12. A method as claimed in claim 11, wherein the liposomal preparation comprises large liposomes and medium liposomes.

30 13. A method as claimed in claim 11, wherein the liposomal preparation comprises medium liposomes and small liposomes.

35 14. A method as claimed in claim 11, wherein the liposomal preparation comprises small, medium and large liposomes.

40 15. A method as claimed in claim 1, wherein the liposomes comprise at least one antigen selected from the group consisting of hepatitis B and hepatitis C antigens.

45 16. A method as claimed in claim 15, wherein the liposomal preparation comprises large liposomes and medium liposomes.

50 17. A method as claimed in claim 15, wherein the liposomal preparation comprises medium liposomes and small liposomes.

55 18. A method as claimed in claim 15, wherein the liposomal preparation comprises small, medium and large liposomes.

19. A method as claimed in claim 1 wherein the at least one antigen is selected from the group of antigens consisting of polio 1, 2, 3; hepatitis A through N; coxsackie B1-
5 B6; mumps; measles; rubella; respiratory syncytial virus; parainfluenza 1-4; influenza A; influenza B; influenza C; adenovirus; mycoplasma pneumonia; streptococcus pneumonia; mycoplasma pneumonia; chlamydia trachomatis; pneumoniae; psittacocci; hemophilus; influenza; meningococcus; malaria; leishmanie; brucella; trypanosoma brucei strains;
10 mycobacterium tuberculosis; pseudomonas; escherichia coli; salmonella; trypanosoma cruzi; yellow fever virus and vibrio cholerae.

20. A method according to claim 1 wherein a the antigen containing liposomes are capable of being absorbed in the Peyer's patches of the gut of the mammal and are
15 capable of being taken up by macrophages in the Peyer's patches to stimulate a systemic immune response without the presence of an adjuvant.

21. A method according to claim 1 wherein the antigen containing liposomes are capable of being absorbed in the Peyer's patches of the gut of the mammal and are capable
20 of being taken up by macrophages in the Peyer's patches to stimulate a systemic immune response without generating a typical adjuvant effect.

22. A method according to claim 1, wherein the liposomal preparation is prepared
25 by:

preparing a plurality of liposomes containing the at least one antigen; and
reducing the size of a portion of the liposomes to produce liposomes having a size
selected from small liposomes and medium liposome, wherein a remainder of the liposomes
are not altered so that the remainder of the liposomes have a size selected from medium
30 liposomes and large liposomes, wherein the size of the remainder of the liposomes is different from the reduced size of the portion of liposomes.

23. A method according to claim 22, wherein the portion of the liposomes are
35 altered to produce small liposomes.

24. A method according to claim 23, wherein the remainder of liposomes that
are not altered are all large liposomes.

5 25. A method according to claim 23, wherein the remainder of liposomes that
are not altered are all medium liposomes.

26. A method according to claim 22, wherein the portion of the liposomes are
10 altered to produce medium liposomes.

27. A method according to claim 26, wherein the remainder of liposomes that
are not altered are all large liposomes.

15 28. A method according to claim 22, wherein the size of the portion of the
liposomes is reduced by sonication.

29. A method according to claim 22, wherein the size of the portion of the
liposomes is reduced by extrusion through a filter.

20 30. A method according to claim 22, wherein the size of the portion of the
liposomes is reduced by microfluidization.

31. A method according to claim 1, wherein the liposomal preparation is
25 prepared by:

preparing a plurality of liposomes containing the at least one antigen;
reducing the size of a first portion of the liposomes to produce small liposomes; and
reducing the size of a second portion of the liposomes to produce medium
liposomes.

30 32. A method according to claim 31, wherein the sizes of the first and second
portions of the liposomes are reduced by sonication.

33. A method according to claim 31, wherein the sizes of the first and second
35 portions of the liposomes are reduced by extrusion through a filter.

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34. A method according to claim 31, wherein the sizes of the first and second
portions of the liposomes are reduced by microfluidization.

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